Amendments to the Claims

Please cancel claims 2-4, 6-8, 12, and 16-18 without prejudice.

The following listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

1. (currently amended) A process to prepare an injectable sustained release pharmaceutical composition comprising:

preparing biodegradable porous microspheres comprising ~~accessible ionic~~cationic functional groups from a mixture of a biocompatible material comprising cationic functional groups and a biodegradable polymer;~~,~~

adding a solution comprising a biopharmaceutical compound to the biodegradable porous microspheres;

incorporating ~~a~~ the biopharmaceutical compound into the biodegradable porous microspheres through ionic interaction by suspending or equilibrating the biodegradable porous microspheres in a solution comprising the biopharmaceutical compound at a pH beyond the pI of the biopharmaceutical compound; and

recovering and freeze-drying the biopharmaceutical-incorporated microspheres; ~~and~~

wherein the biopharmaceutical compound is over 5,000 dalton and is present in an amount of more than 10% by weight.

Claims 2-4 (cancelled)

5. (previously presented) The process of claim 1, wherein the biodegradable porous microsphere comprises one or more of polylactides, polyglycolides, poly(lactide-co-glycolide)s, polycaprolactone, polycarbonates, polyesteramides, polyanhydrides, poly(amino acids), polyorthoesters, polyacetyls, polycyanoacrylates, polyetheresters, poly(dioxanone)s, poly(alkylene alkylate)s, copolymers of polyethylene glycol and polyoithoester, biodegradable polyurethanes, proteins such as albumin, casein, collagen, fibrin, fibrinogen, gelatin, hemoglobin, transfferin, and zero polysaccharides such as alginic acid, chitin, chitosan, chondroitin, dextrin, dextran, hyaluronic acid, heparin, keratmi sulfate, starch and derivatives or blends thereof.

Claims 6-8 (cancelled)

9. (currently amended) The process of claim ~~3~~1, wherein the cationic functional groups comprise primary, ~~binary~~secondary, ternary, or quaternary amine groups.

10. (currently amended) The process of claim ~~3~~1, wherein the ~~biodegradable porous microspheres comprising cationic functional groups~~ biocompatible material comprises a cationic surfactant. ~~and/or biocompatible materials comprising cationic functional group with biodegradable polymer.~~

11. (previously presented) The process of claim 10, wherein the cationic surfactant comprises benzalkonium chloride, benzethonium chloride, or cetrimide.

Claim 12 (cancelled)

13. (currently amended) The process of claims 1, wherein preparing biodegradable porous microspheres comprising ~~ionic~~ cationic functional groups comprises solvent extraction or evaporation in aqueous or organic phase, phase separation, spray drying, low temperature casting, and supercritical gas fluid method.

14. (currently amended) The process of claim 1, wherein porosity of the biodegradable porous microspheres comprising ~~ionic~~ cationic functional groups is increased by addition of gas forming agents or salts such as sodium chloride, calcium chloride, and ammonium bicarbonate during microsphere preparation process.

15. (currently amended) The process of claim 1, wherein preparing the biodegradable porous microspheres comprising ~~ionic~~ cationic functional groups comprises co-addition of:

acidifying agents, wherein the acidifying agents comprise ~~such as~~ lactic acid, glycolic acid, tartaric acid, citric acid, fumaric acid, and malic acid~~,~~; and

alkalizing agents, wherin the alkalizing agents comprise ~~such as~~ diethanolamine, mono ethanolamine, potassium citrate, sodium bicarbonate, calcium carbonate, magnesium carbonate, magnesium oxide, magnesium trisilicate, sodium citrate, meglumine, and triethanolamine and salts.

Claims 16-18 (cancelled)

19. (currently amended) The process of claim 1, ~~wherein the injectable sustained release pharmaceutical composition~~ further ~~comprises~~ comprising coating the composition with one or more of gelatin, fibrin, or albumin.

20. (currently amended) The process of claim 1, wherein the size of the biodegradable porous microspheres is within the range from 0.01 to 500 p,m.

21. (currently amended) An injectable sustained release pharmaceutical composition, comprising:

a biodegradable porous microsphere, comprising ~~accessible ionic~~cationic functional groups from a mixture of a biocompatible material comprising cationic functional groups and a biodegradable polymer; ~~and~~

a biopharmaceutical compound, wherein the biopharmaceutical compound is positioned in the biodegradable porous microsphere.; and

wherein the biopharmaceutical compound is over 5,000 dalton and is present in an amount of more than 10% by weight.

22. (currently amended) The process of claim ~~1~~21, wherein the biodegradable porous microsphere comprises one or more proteins, and wherein the one or more proteins comprise ~~such as~~ albumin, casein, collagen, fibrin, fibrinogen, gelatin, hemoglobin, transfferin, or blends thereof.

23. (currently amended) The process of claim ~~1~~21, wherein the biodegradable porous microsphere comprises one or more of zero polysaccharides, and wherein the one or more zero polysaccharides comprises ~~such as~~ alginic acid, chitin, chitosan, chondroitin, dextrin, dextran, hyaluronic acid, heparin, keratmi sulfate, starch, and derivatives or blends thereof.

24. (currently amended) The composition of claim 21, further comprises a cationic biopharmaceutical compound positioned in the biodegradable porous microspheres comprising anionic functional groups and wherein the pH of an incorporation solution is lower than the pI of the biopharmaceutical compound.

25. (currently amended) The composition of claim 21, further comprises an anionic biopharmaceutical compound positioned in the biodegradable porous microspheres comprising cationic functional groups, wherein the pH of incorporation solution is higher than the pI of the biopharmaceutical compound.

26. (currently amended) The composition of claim 21, wherein the biopharmaceutical compound is present in an amount from 0.1 % to 90 % weight.

27. (previously presented) The composition of claim 21, wherein the biodegradable porous microsphere comprises one or more of polylactides, polyglycolides, poly(lactide-co-glycolide)s, polycaprolactone, polycarbonates, polyesteramides, polyanhydrides, poly(amino acids), polyorthoesters, polyacetyls, polycyanoacrylates, polyetheresters, poly(dioxanone)s, poly(alkylene alkylate)s, copolymers of polyethylene glycol and polyoithoester, biodegradable polyurethanes, proteins such as albumin, casein, collagen, fibrin, fibrinogen, gelatin, hemoglobin, transfferin, and zero polysaccharides such as alginic acid, chitin, chitosan, chondroitin, dextrin, dextran,.hyaluronic acid, heparin, keratmi sulfate, starch and derivatives or blends thereof.

28. (previously presented) The composition of claim 24, wherein the anionic functional groups comprise carboxyl, sulfonyl or phosphoryl groups.

29. (previously presented) The composition of claim 24, wherein the anionic functional groups comprise an anionic surfactant and/or biocompatible materials comprising anionic functional group with biodegradable polymer.

30. (previously presented) The composition of claim 29, wherein the anionic surfactant comprises docusate sodium or sodium lauryl sulfate.

31. (previously presented) The composition of claim 25, wherein the cationic functional groups comprise primary, binary, ternary, or quaternary amine groups.

32. (currently amended) The composition of claim 30, wherein the ~~biodegradable porous microspheres comprising cationic functional groups~~biocompatible material comprises a cationic surfactant. ~~and/or biocompatible materials comprising cationic functional group with biodegradable polymer.~~

33. (currently amended) The composition of claim ~~21~~32, wherein the cationic surfactant comprises benzalkonium chloride, benzethonium chloride, or cetrimide.

34. (previously presented) The composition of claim 21, wherein the biopharmaceutical comprises growth hormones, interferons, colony stimulating factors, interleukins, macrophage activating factors, macrophage peptides, B cell factors, T cell factors, protein A, suppressive factor of allergy, suppressor factors, cytotoxic glycoprotein, immunocytotoxic agents, immunotoxins, imrnunotherapeutic polypeptides, lymphotoxins, tumor necrosis factors, cachectin, oncostatins, tumor inhibitory factors, transforming growth factors, albumin and its fragments, alpha I antitrypsin, apolipoprotein-E, erythroid potentiating factors, erythropoietin, factor VII, factor VIII, factor IX, fibrinolytic agent, hemopoietm-1, kidney plasminogen activator, tissue plasminogen activator, urokinase, prourokinase, streptokinase, lipocortin, lipomodulin, macrocortin, lung surfactant protein, protein C, protein 5, C-reactive protein, renin inhibitors, collagenase inhibitors, superoxide dismutase, epidermal growth factor, platelet derived growth factor, osteogenic growth factors, atrial naturetic factor, auriculin, atriopeptin, bone morphogenetic protein, calcitonin, calcitonin precursor, calcitonin gene-related peptide, cartilage inducing factor, connective tissue activator protein, fertility hormones (follicle stimulating hormone, leutinizing hormone, human chorionic gonadotropin), growth hormone releasing factor, osteogenic protein, insulin, proinsulin, nerve growth factor, parathyroid hormone, parathyroid hormone inhibitors, relaxin, secretin, somatomedin C, insulin-like growth factors, inhibin, adrenocorticotrophic hormone, glucagons, vasoactive intestinal polypeptide, gastric inhibitory peptide, motilin, cholecystoldnin, pancreatic polypeptide, gastrin releasing peptide, corticotropin releasing factor, thyroid stimulating hormone, or vaccine antigens of, and anti-infective antibodies to, bacterial or viral or other infectious organisms and mutants or analogs thereof.

35. (previously presented) The composition of claim 21, further comprises a coating.

36. (previously presented) The composition of claim 35, wherein the coating comprises one or more of gelatin, fibrin, or albumin.